09/830807

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450 Alexandria, VA 22313 on February 10, 2005

Glenn P. Ladwig

Glenn P. Ladwig, Patent Attorney

REQUEST FOR CERTIFICATE OF CORRECTION UNDER 37 CFR 1.322 and 1.323
Docket No. GJE-65
Patent No. 6,846,667

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	Crooke *et al.*
Issued	:	January 25, 2005
Patent No.	:	6,846,667
For	:	Virulence Genes and Proteins, and Their Use

ATTN: CERTIFICATE OF CORRECTIONS BRANCH
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REQUEST FOR CERTIFICATE OF CORRECTION UNDER 37 CFR 1.322 (OFFICE MISTAKE) AND UNDER 37 CFR 1.323 (APPLICANTS' MISTAKE)

Sir:

A Certificate of Correction for the above-identified patent has been prepared and is attached hereto.

In the left-hand column below is the column and line number where errors occurred in the patent. In the right-hand column is the page and line number in the application where the correct information appears.

Patent Reads:	**Application Should Read:**
Column 1, Line 4: "[BLANK]"	Page 1, Line 2: -- Cross-Reference to Related Application This application is the National Stage of International Application Number PCT/GB99/03721, filed November 9, 1999.--
Patent Reads:	**Application Reads:**
Column 137, Line 24: "tatE, or the obtainable"	See Amendment dated 06/23/04; Claim 23, line 8: --tatE, obtainable--
Column 138, Lines 14-15: "bacterium nucleotide or amino acid level."	See Amendment dated 06/23/04; Claim 23, line 8: --bacterium.--

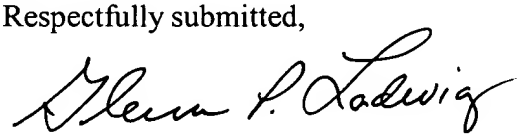
A true and correct copy of the applicants' Amendment dated June 23, 2004 which supports the applicants' assertion of errors on the part of the Patent Office accompanies this Certificate of Correction.

The addition of the cross-reference section to page 1 of the application, indicating that the application is a National Stage of International Application Number PCT/GB99/03721, filed November 9, 1999, is consistent with the Official Filing Receipt and the Declaration of record.

The Commissioner is authorized to charge the fee of $100.00 for the amendment to Deposit Account No. 19-0065. The Commissioner is also authorized to charge any additional fees as required under 37 CFR 1.20(a) to Deposit Account No. 19-0065. Two copies of this letter are enclosed for Deposit Account authorization.

Approval of the Certificate of Correction is respectfully requested.

Respectfully submitted,



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Fax No.: 352-372-5800
Address: P.O. Box 142950
Gainesville, FL 32614-2950

GPL/mv
Attachments: Certificate of Correction in duplicate
Copy of applicants' Amendment dated June 23, 2004
Two copies of this letter

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FEB 28 2005

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COPY

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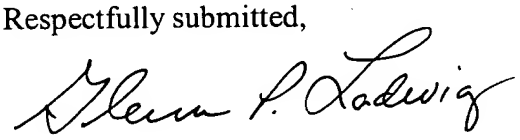

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Copy of applicants' Amendment dated June 23, 2004
Two copies of this letter

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 6,846,667

DATED : January 25, 2005

INVENTORS : Crooke *et al.*

It is certified that errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

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Line 4, should read -- Cross-Reference to Related Application
This application is the National Stage of International Application Number PCT/GB99/03721, filed November 9, 1999.--

Column 137
Line 24, "tatE, or the obtainable" should read --tatE, obtainable--.

Lines 14-15, "bacterium nucleotide or amino acid level." should read --bacterium.--.

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PATENT NO. 6,846,667

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UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

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DATED : January 25, 2005

INVENTORS : Crooke *et al.*

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PATENT NO. 6,846,667

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I hereby certify that this correspondence is being facsimile transmitted to the United States Patent and Trademark Office on June 23, 2004.

Glenn P. Ladwig

Glenn P. Ladwig, Patent Attorney

AMENDMENT UNDER 37 C.F.R. § 1.116
Examining Group 1645
Patent Application
Docket No. GJE-65
Serial No. 09/830,807

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Examiner	:	Jana A. Hines
Art Unit	:	1645
Applicants	:	Helen Rachel Crooke, Enda Elizabeth Clarke, Paul Howard Everest, Gordon Dougan, David William Holden, Jacqueline Elizabeth Shea, Robert Graham Feldman
Serial No.	:	09/830,807
Filed	:	April 30, 2001
Confirm. No.	:	2112
For	:	Virulence Genes and Proteins, and Their Use

MS AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

AMENDMENT UNDER 37 C.F.R. §1.116

A Petition and fee for a one-month Extension of Time through and including July 16, 2004, accompanies this Amendment.

In response to the Office Action dated March 16, 2004, please amend the above-identified application as follows:

In the Claims

Claims 1-8 and 9-22 (Cancelled)

Claim 23 (Currently amended): A method for screening a potential drug using a peptide, said method comprising:

contacting the peptide with the potential drug, wherein the peptide has the ability to translocate a protein from the bacterial cytoplasm to the periplasm; and

determining whether the potential drug inhibits the ability of the peptide to translocate a protein from the bacterial cytoplasm to the periplasm, wherein the peptide ~~is obtainable from *E. coli* K1 and~~ is encoded by ~~an operon comprising~~ a gene selected from the group consisting of *tatA*, *tatB*, *tatC*, and *tatE*, ~~or a homologue or functional fragment of any of the foregoing, wherein the homologue is~~ obtainable from a Gram-negative bacterium ~~and has at least 30% homology at the nucleotide or amino acid level~~.

Claims 24-26 (Cancelled)

Claim 27 (Currently amended): The method of claim 23, wherein the ~~operon comprises the *tatB* gene~~ peptide is encoded by the *tatB* gene.

Claim 28 (Cancelled)

Claim 29 (Previously added): The method of claim 23, wherein the peptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, and SEQ ID NO:15.

Claims 30-33 (Cancelled)

Claim 34 (Previously added): The method of claim 23, wherein the peptide comprises the amino acid sequence of SEQ ID NO:12.

Claims 35-40 (Cancelled)

Remarks

Claims 9 and 23-40 were pending in the subject application. By this Amendment, claims 23 and 27 have been amended and claims 9, 24-26, 28, 30-33, and 35-40 have been cancelled. The undersigned avers that no new matter is introduced by this amendment. Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 23, 27, 29, and 34 are currently before the Examiner for consideration. Favorable consideration of the pending claims is respectfully requested.

Claim 9 has been rejected under 35 U.S.C. §112, second paragraph, as incomplete for omitting essential steps. The applicants have cancelled claim 9, thereby rendering this rejection moot. Reconsideration and withdrawal of the rejection under 35 U.S.C. §112, second paragraph, is respectfully requested.

Claims 9 and 23-40 are rejected under 35 U.S.C. §112, first paragraph, as lacking sufficient written description and as new matter. The applicants respectfully submit that the subject specification provides sufficient written description for claims 9 and 23-40. However, by this Amendment, the applicants have cancelled claim 9, and amended claim 23 to lend further clarity to the claimed subject matter.

The Office Action asserts that the subject specification does not provide an adequate written description of homologues or functional fragments of *tatA*, *tatB*, *tatC*, *tatE*, or SEQ ID NOs:11, 12, 13, or 15. The applicants have amended claim 23 to delete reference to homologues or functional fragments.

The Office Action indicates that the subject specification does not provide an adequate written description of a method for screening potential drugs by contacting the recited peptide with the potential drug and determining whether the potential drug inhibits the ability of the peptide to translocate a protein from the bacterial cytoplasm to the periplasm. The applicants respectfully submit that the steps recited in claim 23 are implicit within the disclosure of the subject specification. The fundamental factual inquiry for sufficiency of written description is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed. The subject matter of the claim need not be described literally (*i.e.*, using the

same terms or *in haec verba*) in order for the disclosure to satisfy the written description requirement. Information that was well known to persons of ordinary skill in the art need not be included in the application and preferably, is omitted. *In re Buchner*, 18 USPQ 2d 1331 (Fed. Cir. 1991). Furthermore, it is well settled that by disclosing a device that inherently performs a function or has a property, operates according to a theory or has an advantage, the patent application necessarily discloses that function, theory or advantage, even though it says nothing explicit concerning it. Thus, the application may later be amended to recite the function, theory or advantage without introducing prohibited new matter. *In re Reynolds*, 170 USPQ 94 (CCPA 1971); *In re Smythe*, 178 USPQ 279 (CCPA 1973); and MPEP §2163.07(a).

The role of Tat proteins in translocation was known prior to the filing of the subject application. Moreover, the subject specification teaches that the *tat* system is a *Sec*-independent export pathway that permits translocation of fully folded proteins to the periplasm through a gated pore (page 9, lines 5-9 of the specification) and that the genes and encoded peptides disclosed therein can be used as targets for screening potential drugs (page 2, lines 15-17; page 5, lines 5-7). One of ordinary skill in the art is provided with adequate information regarding the biological activity of the Tat proteins.

The concept underlying the invention is the finding that the Tat proteins are implicated in virulence and that therefore the proteins, or the genes encoding the proteins, are useful targets for antimicrobial therapy. One of ordinary skill in the art reading the whole specification would appreciate that the Tat proteins are useful targets for antimicrobials. Therefore, it is not difficult for one skilled in the art to extend this to evaluating different compounds for their ability to inhibit Tat activity. Once one of ordinary skill in the art is taught that a Tat peptide is an anti-microbial target, standard techniques in the art are immediately envisioned to utilize the peptide in a screen, to identify drugs that alter its natural biological function; it is merely a question of measuring the natural activity of the peptide. A screening assay for antimicrobial drugs merely has to determine whether a drug has the ability to inhibit or alter the natural biological function of a Tat protein. One of ordinary skill in the art can be reasonably expected to know how Tat activity can be determined, in view of the existing knowledge of the Tat export pathway (*e.g.*, Tat proteins and Tat substrates). For example, the Materials and Methods section of the Lee *et al.* publication (page 5873), which was

submitted to the Patent Office with the previous Response on December 15, 2003, indicates that translocation activity of truncated forms of TatA and TatB polypeptides was assessed by measuring trimethyl amine *N*-oxide (TMAO) reductase activity, and cites a 1988 publication (Silvestro *et al.*, *Biochim. Biophys. Acta* 954:1-13) which discloses the methodology. Other Tat substrates could also be utilized. Therefore, there is sufficient information provided within the specification so as to allow the skilled person to carry out a screening assay as recited in the claim.

The applicants respectfully submit that the subject specification reasonably conveys to one of ordinary skill in the art that the inventors were in possession of the claimed invention, and the claimed methods do not represent new matter. Accordingly, reconsideration and withdrawal of the rejections under 35 U.S.C. §112, first paragraph, is respectfully requested.

Claims 9 and 23-40 are rejected under 35 U.S.C. §112, first paragraph, as non-enabled by the subject specification. The applicants respectfully submit that the claimed invention is fully enabled by the subject specification.

As indicated above, the applicants have cancelled claims 9, 24-26, 28, 30-33, and 35-40. With regard to claims 23, 27, 29, and 34, once one of ordinary skill in the art is taught that a specific peptide, such as a Tat peptide, is an anti-microbial target, standard techniques in the art are simple to apply in order to utilize the peptide in a screen, to identify drugs that inhibit its natural biological function. Measuring the activity of a peptide may require significant experimentation if its function is not known, but the Tat peptide's function was known and is indicated in the specification. Moreover, assays for measuring the activity of the Tat peptide are well known, as evidenced by the Lee *et al.* publication (page 5873).

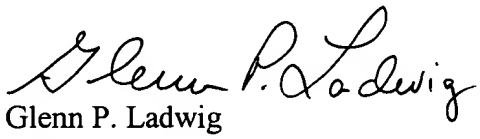
The techniques and materials required for carrying out the method of the invention were known and readily available. Thus, one of ordinary skill in the art would not have to resort to undue experimentation to carry out the invention. "The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine..." *In re Wands*, 8 USPQ 2d 1400, 1404 (Fed. Cir. 1988) (citing *in re Angstadt*, 190 USPQ 214, 217-219 (CCPA 1976)). Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph, is respectfully requested.

In view of the foregoing remarks and amendments to the claims, the applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16 or 1.17 as required by this paper to Deposit Account 19-0065.

The applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



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